



## Clinical trial results:

**Estrategias para mejorar la eficacia y seguridad del tratamiento con Simvastatina en la Fase Aguda del Ictus Isquémico: STARS trial.**

**Improving Safety and Efficacy of Simvastatin Treatment for the Acute Phase of Ischemic Stroke: STARS trial.**

### Summary

EudraCT number	2007-005868-26
Trial protocol	ES
Global end of trial date	10 March 2014

### Results information

Result version number	v1 (current)
This version publication date	20 October 2021
First version publication date	20 October 2021
Summary attachment (see zip file)	Stroke2016 Montaner (STROKEAHA.116.014600.pdf)

### Trial information

#### Trial identification

Sponsor protocol code	stars07
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01073007
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, joaquin.lopez.soriano@vhir.org
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Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 March 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 March 2014
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Demostrar que en la fase aguda del ictus isquémico el tratamiento con Simvastatina administrado en las primeras 12h del inicio de los síntomas mejora la situación neurológica y funcional del paciente valorado a los 7 días y tercer mes del inicio del tratamiento.

[To demonstrate that in the acute phase of ischemic stroke, Simvastatin given within 12 hours of stroke onset improves neurological and functional status evaluated at day seven (or at discharge if this occurs before day 7) and at three months respectively].

Protection of trial subjects:

Neurological deterioration (increase of the NIHSS  $\geq 4$  points) and major neurological improvement (NIHSS score of 0 or decrease in the NIHSS score,  $\geq 8$ ) were assessed at 7 days.

Background therapy:

Intravenous tPA.

Evidence for comparator: -

Actual start date of recruitment	03 March 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	20

From 65 to 84 years	84
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details: -

### Pre-assignment period milestones

Number of subjects started	104
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Number of subjects completed	104
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### Period 1

Period 1 title	Overall trial (overall period)
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Is this the baseline period?	Yes
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Allocation method	Randomised - controlled
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Blinding used	Double blind
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Roles blinded	Subject, Investigator
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### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	Placebo
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Arm description: -

Arm type	No intervention
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No investigational medicinal product assigned in this arm

<b>Arm title</b>	Simvastatin
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Arm description: -

Arm type	Active comparator
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Investigational medicinal product name	Simvastatin
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for injection
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Routes of administration	Intravenous use
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Dosage and administration details:

40 mg once daily for 90 days

Number of subjects in period 1	Placebo	Simvastatin
Started	54	50
Completed	50	48
Not completed	4	2
Lost to follow-up	4	2

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	104	104	
Age categorical			
Units: Subjects			
Adults (18-64 years)	20	20	
From 65-84 years	84	84	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	74		
inter-quartile range (Q1-Q3)	62.5 to 82	-	
Gender categorical			
Units: Subjects			
Female	48	48	
Male	56	56	

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Simvastatin
Reporting group description: -	
Subject analysis set title	Complete treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
Rankin Scale score	

### Primary: Rankin scale

End point title	Rankin scale
End point description:	
End point type	Primary
End point timeframe:	
At the end of the treatment	

End point values	Placebo	Simvastatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	48		
Units: unit(s)				
number (not applicable)				
Under 2	35	33		

### Statistical analyses

Statistical analysis title	Rankin scale
Comparison groups	Placebo v Simvastatin
Number of subjects included in analysis	98
Analysis specification	Post-hoc
Analysis type	superiority
P-value	= 0.98
Method	t-test, 1-sided

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

All the study

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.1
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### Reporting groups

Reporting group title	Total adverse events
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: All the reported adverse events were considered as serious. Non-serious events were not reported in the final publication (no additional data available)

Serious adverse events	Total adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 104 (11.54%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Heart failure			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angor			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Malignant edema			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Neurological deterioration			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Symptomatic intracerebral hemorrhage			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Meningitis			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Delirium			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
CRA branch occlusion			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory infection			



subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchial aspiration procedure			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 104 (1.92%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyponatraemia			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Total adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 104 (0.00%)		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Because of the low recruitment, the STARS trial was underpowered to detect differences in simvastatin efficacy.
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Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/27758944>